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# *The* Journal of Infectious Diseases

FOUNDED BY THE MEMORIAL INSTITUTE FOR INFECTIOUS DISEASES

VOL. 6

February 18, 1909

No. 1

## THE EPITHELIAL CELL CHANGES IN MEASLES.\*

JAMES EWING.

(From Cornell University Medical College, New York City.)

NEUMANN<sup>1</sup> in 1880, writing on the subject of the histology of measles, expressed his surprise that so little attention had been paid to this interesting subject. The only definite observation which he was able to find was that of Cornil and Ranvier<sup>2</sup> who described in the skin engorgement of the vessels and the presence of some wandering cells and pigment granules in the papillae and Malpighian layer. Contrary to Cornil, Neumann did not detect any leucocytes in the epithelium, but found the cellular infiltration limited to the subepithelial tissue and localized in a rather specific manner about the hair follicles and sebaceous and sweat glands. Likewise Mayr,<sup>3</sup> as well as Hebra,<sup>4</sup> located the morbid process chiefly in the sebaceous glands, finding the hair follicles only occasionally and accidentally involved. Kaposi<sup>5</sup> dismissed the subject with the statement that the microscope

\* Received for publication November 15, 1908.

<sup>1</sup> *Med. Jahrb.*, 1882, p. 157.

<sup>2</sup> *Anat. Path.*, 2, p. 701; also *Path. Hist.*, London, 1886, 2, p. 651.

<sup>3</sup> *Hebra's Diseases of Skin*, London, 1866, 1, p. 177.

<sup>4</sup> *Lehrbuch d. Hautkrankheiten*, Erlangen, 1872, 2, p. 137.

<sup>5</sup> *Path. et Traité des malad. de la peau*, Paris, 1891, 1, p. 250.

had not been able to show, either in the epidermis or in the papillae, any lesion which pointed to a proliferation of cells.

The first report of a definite effort to examine in detail and with competent methods the cutaneous lesions of measles appears to be that of Catrin,<sup>1</sup> who in 1890 presented a full report of the study of a single case coming to autopsy on the fourth day at the height of a maculo-papular eruption. His general conclusion was that the localized maculo-papular lesions reduce themselves purely and simply to a lymphoid infiltration about the arterioles, the hair follicles, and the sebaceous and sweat glands. In addition to this process, which had been recognized by others, he added the description of a new lesion in the form of vesicles, "phlyctenes," in various stages of development. Some of these were superficial and consisted of a separation of the epithelial layers between the stratum granulosum and the deeper layers, while others, the more specific, were located between the Malpighian layer and the derma, the papillae of the derma forming the floor of the vesicle.

In the formation of these vesicles Catrin traced the influence of a peculiar colloid degeneration of the epithelial cells, coagulation necrosis, and slight serous exudation. Beneath the vesicles the glandular structures usually showed cellular infiltration and the combination of these lesions produced the large elevated papules of "rougeole boutonneuse."

Finally Catrin described certain epithelial lesions which he regarded as specific of measles. The first of these consisted of the formation of colloid masses about the nuclei. These appeared first in the form of a single homogeneous globule at one side of the nucleus which increased in size, pushed the nucleus aside, or completely enveloped it, and eventually came to occupy a large portion of the cell or even distended its borders. By the fusion of these globules from adjoining cells large masses of colloid matter of mulberry form were sometimes produced. Associated with advanced stages of this colloid degeneration he noted increasing infiltration of the epidermis with lymphoid cells and coagulation necrosis of strands of cells producing at times a mass of necrotic epithelium isolated by lymphoid cells and a slight amount of serum. In the fresh condition the colloid globules ap-

\* *Arch. de méd. expér.*, 1891, 3, p. 197.

peared like masses of gelatine and in sections of tissue they stained brick red with eosin.

Catrin mentioned that in one of his sections he observed in the pustules brilliantly stained ovoid bodies with large nuclei which he thought were evidently micro-organisms different in type from the schizomycetes.

Hlava,<sup>1</sup> 1906, excised Koplik's spots from the mucous membrane of the cheek in five cases of measles, and described two types of changes: (1) A parakeratosis or complete keratinization of the superficial layers with subsequent desquamation. This process he regarded as identical with the ordinary exanthem of measles; (2) A focal necrosis of the basal epithelial cells, with colliquation and formation of a vesicle or pustule which was surrounded by a superficial layer of keratinized cells. These circumscribed foci surrounded by a hyperemic zone correspond to Koplik's spots, which therefore represent a pustular measles eruption. From this report and from the observations on the present cases it would appear that the exact histology of Koplik's spots varies as does that of the general exanthem of measles. The term pustule does not accurately designate any of these lesions, since polynuclear leucocytes are scanty or absent in these foci.

In Gervalas'<sup>2</sup> study of one case no specific changes in the skin were observed, but numerous cocci were found in the cutaneous structures.

In recent years additional interest would seem to attach to the minute histology of the lesions of the skin in measles owing to the fact that many studies of the lesions in other members of the group of exanthemata have appeared, especially of smallpox and lately of scarlet fever, in which the authors have described intracellular bodies which they believed to be protozoa.

It was from this latter point of view that I began in 1902 to collect and study material from cases of measles, and it is the object of this report to present the results of this study. The material has been collected slowly and with difficulty as the disease is not commonly fatal during the period of eruption. The first case was secured in 1902 at the Willard Parker Hospital through the kindness of Dr. W. H. Park, and several others were obtained at the New York Foundling

<sup>1</sup> *Casopis lék česk.*, Prague, 1906, 45, p. 773, cit. in *Schmidt's Jahrb.*, 1906, 291, p. 242.

<sup>2</sup> *Allg. Wien. med. Ztschr.*, 1906, 51, p. 421.

Hospital through the co-operation of Dr. John Howland and Dr. Matthias Nicoll. The immediate incentive to the preparation of this report arose when Dr. Anna W. Williams of the New York Board of Health very kindly placed at my disposal prepared tissues taken from three patients during life. In this way the report comes to cover the study of nine cases of measles, on post-mortem material in six cases, and on Dr. Williams' material in three cases. For the assistance secured from all of these sources I take pleasure in expressing my thanks and obligation.

#### TECHNIC.

The tissues were fixed in various reagents, including Orth's fluid, Zenker's fluid,  $HgCl_2$ , and alcohol (50 per cent). Paraffin sections were stained with eosin and hematoxylin, eosin and methylene blue, eosin and polychrome methylene blue (Nocht's method), iodin green and fuchsin (Borrell's method), gentian violet, and Gram's method for bacteria.

#### DESCRIPTION OF LESIONS.

The changes observed in the skin in these cases constitute three rather distinct series, one of which is represented by a single case, one by two cases, while the remaining six cases fall in a group which seems to represent the more common lesions of measles.

*Case 1.*—Willard Parker Hospital. Autopsy six hours after death, by the writer. The body is of a well-nourished male child about four years of age. It is covered by a profuse general brownish maculo-papular eruption, in places over the chest nearly diffuse, elsewhere discrete. There is no appearance of scaling. Heart normal. In the lungs there are intense congestion and mucopurulent bronchitis extending to the finest bronchioles, but no areas of pneumonia. The liver is congested, not fatty, but shows a moderate number of minute focal necroses. The kidneys are pale and of slightly reduced consistence. There is moderate hypertrophy of the solitary and agminated intestinal lymph follicles. Spleen moderately congested.

The chief interest for the present report concerns the histological lesions of the skin, which proved to be of a most noteworthy character (see Figs. 1 and 2). The most striking feature of the epidermis is a marked thickening of the zone of keratosis which appears as a broad hyaline incrustation almost as wide as the Malpighian layer. In this zone appear numerous groups of imperfectly keratinized cells staining dark with methylene blue and representing the early stages of the branny desquamation of the disease. The exact steps in the outward progress of these groups of cells from the Malpighian layer to their observed position I have been unable to follow, nor do I find in the literature a satisfactory explanation of their mode of origin.

The cells of the Malpighian layer present a series of remarkable transformations which I believe to be quite unique and specific. They may best be traced in the drawing (Plate 1, Fig. 1). Almost the entire mass of cell protoplasm and nuclei is broken up into a series of curious figures which includes ring-shaped bodies, homogeneous spherical globules, crescent-shaped masses, and fragments of highly irregular outline. The nuclei are intact but homogeneous, or extensively vacuolated, or broken into fragments which sometimes show vacuoles in geometric arrangement, while the nucleoli are absent or displaced, or shrunken or vacuolated. The cells of the hair follicles and sebaceous glands are similarly affected. Between the epithelia are occasionally seen isolated elongated homogenous cells in coagulation necrosis.

The extent and variety

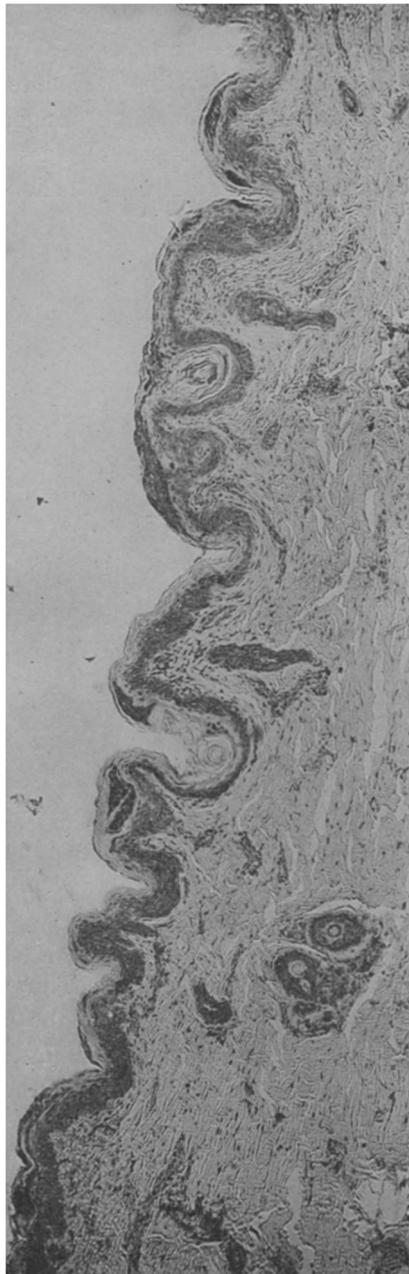


FIG. 1.—Diffuse hyperkeratosis and abundant scale formation in measles (Case 1). Bichloride, eosin, and methylene blue. Specimen shows continuous thick layer of zone of keratosis, in places involving nearly the whole epidermis and containing very numerous dark-staining adherent scales.

of these cellular changes exceed anything I have seen in variola or scarlatina, but in some respects they resemble the peculiar intracellular structures described in these latter diseases. It is difficult to find a phrase which will suitably designate this series of changes but they seem to fall into the general class of degeneration, coagulation necrosis, and disintegration of epithelial cells such as in some degree

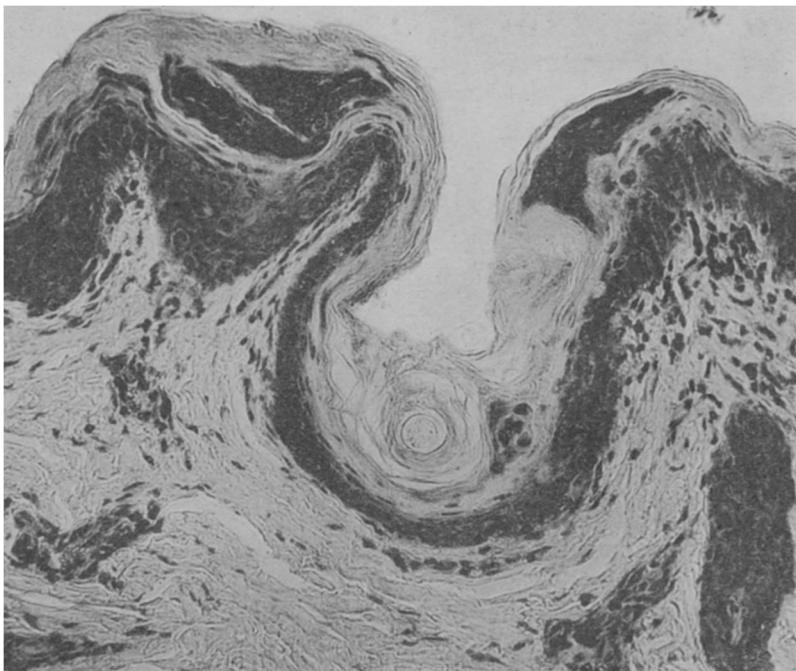


FIG. 2.—The same as Fig. 1, in higher magnification.

characterize all the exanthemata. They would thus seem to represent the reaction of the epithelium to the toxic agents of the disease, and their occurrence in such striking form demonstrates that in measles as in variola and scarlatina the epidermis may react in a specific manner. In a considerable number of other specific diseases of the skin I have been unable to find similar alterations of epithelial cells.

In the mucous membranes the lesions were less striking and peculiar. In the pharynx there is slight general edema of the sub-

mucosa and very numerous collections of round cells. The epithelium shows a marked desquamative process with definite erosions but no distinct ulcers or focal necroses. In the transitional epithelium of the larynx the superficial flat cells are often in coagulation necrosis or keratinization and there is a bulky growth of cocci in and about these superficial cells. The submucosa of the larynx and trachea shows extensive diffuse infiltration by round cells.

*Case 2.—(No. 1897.) Hemorrhagic measles. New York Foundling Hospital. Patient of Dr. Nicoll. Age 2½ years. Died on the fourth day from uncomplicated measles. A complete autopsy was not permitted but portions of skin from the back and abdomen were obtained 12 hours after death, and placed in 50 per cent alcohol.*

The lesions observed in this material were striking and peculiar. They consisted chiefly in the formation of perinuclear vacuoles, single or multiple, large and small, sometimes displacing the nucleus to one side, sometimes completely surrounding the nucleus. Occasionally the vacuoles from adjoining cells were fused and often an elongated vacuole extended some distance between the cells, pushing the cytoplasm ahead as a tongue-like protrusion. These vacuoles contain a faintly basic-staining homogeneous material which is recognizable also by its refractive properties. In the vacuoles also are almost invariably found one or more densely staining basophilic bodies, the origin and nature of which it is difficult to determine. Many of these are very minute, some are large, irregular globules. Definite ring shapes appear and it is possible that some of the minute bodies are parts of larger ring-shaped structures. Some resemble biscuit-shaped diplococci, others resemble elongated pear-shaped cocci. A marked lack of uniformity in size and shape leaves a very confusing impression with the observer. The bodies are not limited to the vacuoles but many are found scattered in the cytoplasm, and the intercellular spaces, especially between the basal cells, may be closely filled with them. Neither are they limited to the epithelial layers, but in the subepithelial lymph spaces and capillaries very numerous collections are found, and they appear also in and about all the epithelial structures of the derma. They are much more numerous than is indicated in the sketch (Plate 1, Fig. 2). They are Gram-negative, and stain densely with gentian violet, and distinctly with strong eosin.

After numerous attacks upon the question I have been unable to reach a satisfactory conclusion as to the nature of these bodies. They are not bacteria. Their numbers and distribution might suggest to some a protozoon hypothesis, as many of the forms show resemblance to the piroplasms. I am more inclined to regard the appearances as the result of coagulation of an albuminous exudate or degenerative product derived from the epithelium. In a considerable series of other diseases of the skin examined for control I have found very similar bodies in and between the epithelial cells in one acute case of *pityriasis rosea*. This disease bears some clinical resemblance to measles.

*Case 3.*—(No. 1966.) New York Foundling Hospital, May 16, 1904. Patient of Dr. Nicoll. Age six years. Died on the fourth day of well-marked maculo-papular eruption with symptoms of broncho-pneumonia. Autopsy by the writer, 36 hours after death.

Anatomical diagnosis: Broncho-pneumonia. Ulcerative stomatitis and pharyngitis. Catarrhal bronchitis. Acute degeneration of liver and kidneys. Abundant fine papular exanthem of measles.

Portions of skin were taken from the trunk, arm, and leg, and hardened in Zenker's fluid. The lesions observed in the skin consisted in the appearance of large vacuoles about the nuclei of cells of the Malpighian layer, the presence of isolated necrotic cells in this layer, and the occurrence of focal points of necrosis of epithelial cells leading to the formation of small vesicles or pustules. The vesicles were often found in connection with similar changes in the sebaceous glands and hair follicles (Figs. 3, 4), these latter structures being nearly always extensively affected.

The minute changes in the necrotic foci are detailed in the colored sketch (Plate 2). There is a small central cavity containing granular coagulum and detached necrosing epithelia. The next adjoining cells show various stages of coagulation necrosis. Beyond these come some isolated necrotic cells, others with large perinuclear vacuoles, while some are but slightly altered. A great variety of peculiar structures is found in the cytoplasm of the degenerating cells, in the perinuclear vacuoles, and between the loosened cells. Most of these are represented in the sketch and it may be said of them that very similar bodies may be found in variolous lesions and in the experimental necrosis of epithelium produced by diphtheria

toxin. Others resemble the structures described in and about the cells in Case 2. In the sweat glands especially there are very numerous perinuclear vacuoles containing minute granules and rings identical with those seen in Case 2 and sketched in Plate 1, Fig. 2.

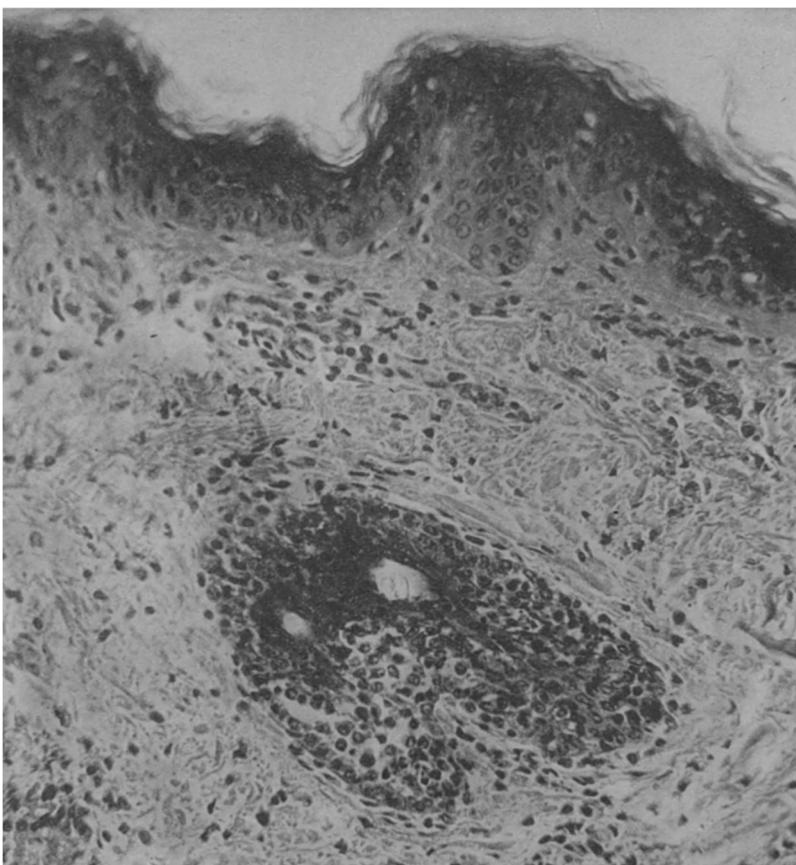


FIG. 3.—Hair follicles of measles (Case 3). Zenker's fluid, eosin, and methylene blue. Specimen shows hydropic vacuoles in epidermis; edema, and increase of large round cells of derma; edema, and various stages of degeneration of cells of hair follicle.

There is a uniform increase in the number of large round cells in the derma, and these seem to be divided among exuded large mononuclear leucocytes and multiplying endothelia. The vesicles are usually capped by a thickened layer of hornified scales. Bacteria could not

be identified in the epithelial layers, but in this as in other cases the more superficial scales always contained a number of cocc.

Mucous membranes. The buccal, pharyngeal, and entire length of the respiratory tract was carefully examined for gross, micro-

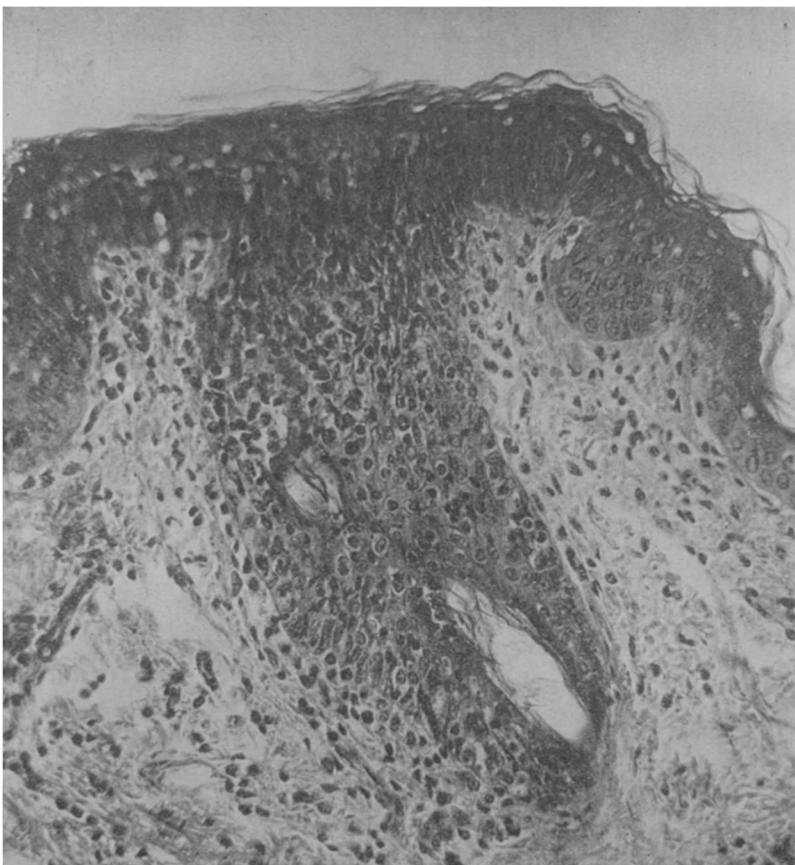


FIG. 4.—Hair follicles of measles (Case 3). Specimen shows extension of lesion of hair follicle into epidermis.

scopical, and minute intracellular changes. There were found the results of a universal intense catarrhal inflammation with marked desquamation of cells, and pronounced infiltration of the submucosa with large and small round cells. In the larynx, trachea, and bronchi the desquamation of lining cells produced occasional erosions down

to the membrana propria or entering the mouths of mucous glands. In the mouth and pharynx there were isolated necrotic cells, general edema, and many small focal necroses in the epithelium, comparable to those of the skin, giving small, crater-like ulcers. The vessels beneath these ulcers were always intensely congested, or filled with densely packed red-cell thrombi. These lesions seem to fall in the class of Koplik's spots (Fig. 5). At a few points in the pharyngeal mucosa there were larger and deeper ulcers covered with fibrinous

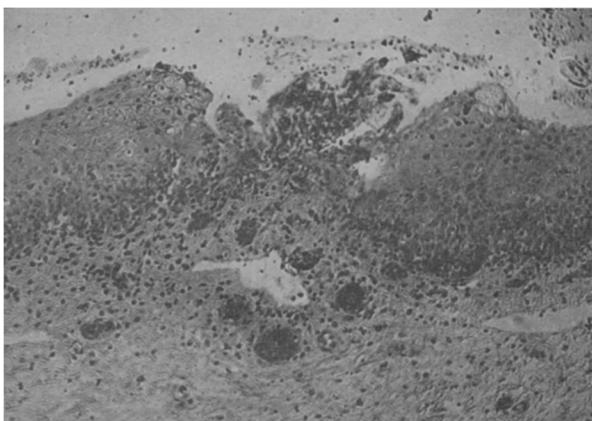


FIG. 5.—Focal ulcer of buccal mucosa in measles (Case 3). Specimen shows a small necrotic focus involving the whole layer of epithelium. The slough is adherent. The submucosa contains small vessels gorged with blood and some round cell infiltration.

membrane (Fig. 6). Throughout the lungs there was intense congestion in interstitial exudative and productive bronchitis and beginning broncho-pneumonia. The liver showed congestion, granular degeneration, and foci of intense fatty degeneration. The kidneys were intensely congested and the tubule cells in marked granular degeneration.

*Case 4.*—New York Foundling Hospital, May 17, 1904. Patient of Dr. Nicoll. Died in the acute eruptive stage of measles, with terminal convulsions. The exact day of the disease was not determined. A complete autopsy was not permitted but portions of skin from the arm and trunk were obtained, which showed a fine maculo-papular eruption.

Microscopical examination showed changes in the skin which were identical in character with those of Case 3. The focal necroses were less numerous, but isolated necrotic cells, edema, and perinuclear vacuolation were rather more noticeable.

*Case 5.*—(1895.) New York Foundling Hospital, February, 1904. Patient of Dr. Howland. Age 4½ years. Died in the early stage of desquamation of measles with symptoms of broncho-pneumonia.

Anatomical diagnosis: Broncho-pneumonia. Acute degeneration of liver and kidneys. Congestion of spleen. Acute pharyngitis and laryngitis. Branny desquamation of skin.

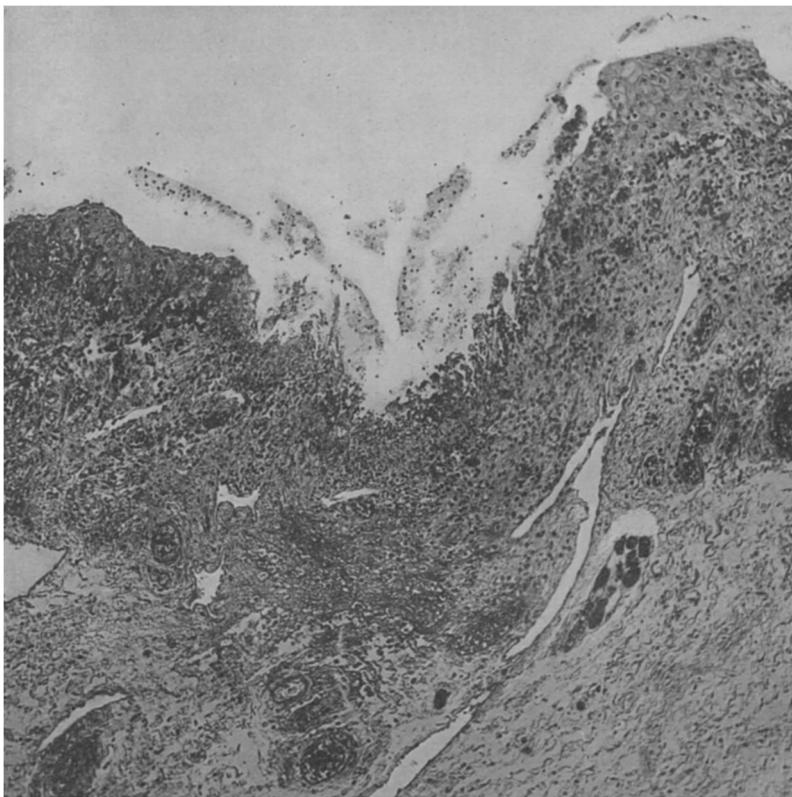


FIG. 6.—Superficial ulcer and diffuse necrosis of lower pharyngeal mucosa (Case 3). There is a large, partly denuded area of epithelium, the necrosis extending at one point into the submucosa. At the left the basal cells show early necrosis. The edge of a second ulcer appears on the right. The blood vessels are distended, and there is edema, fibrinous exudate, and round-cell infiltration of the submucosa.

Microscopical examination: Apart from the presence of many loose desquamating scales there are few changes in the cutaneous epithelium. A good many cells showed mitotic nuclei and a few homogeneous perinuclear bodies were found, but the usual hydropic vacuoles and isolated necrotic cells or necrotic foci were missing. There is considerable congestion of the skin, and some increase of plasma cells, endothelia, and round cells about the basal epithelium vessels and glands. The skin in this case therefore represents the healing stage of measles.

**Pharynx.** There is considerable edema and increase of round cells beneath the epithelial layer and some edema and hydropic degeneration of the epithelium. These changes tend to be focal. At one point a definite area of superficial necrosis covered by fibrin was found. Larynx and trachea show active catarrhal inflammation with extensive desquamation of lining cells and much increase in the round cells beneath the epithelium. At some points near mouths of mucous glands there are superficial erosions. In the bronchi and bronchioles the catarrhal inflammation becomes more intense, there are advanced hydropic degeneration of lining cells and much desquamation. To these changes is finally added, as one reaches the pulmonary parenchyma, an interstitial exudate containing many round cells, and the lesion eventually passes into definite broncho-pneumonia with considerable diffuse exudation into the alveoli. At no point were specific lesions of the epithelial cells observed. The liver shows advanced granular and fatty degeneration, with focal areas of intense fatty degeneration. The kidneys show acute exudative nephritis. The spleen is extensively congested.

**Case 6.**—New York Foundling Hospital, February, 1904. Patient of Dr. Nicoll. Died in the stage of desquamation with symptoms of broncho-pneumonia. The material consisted of portions of skin only, a complete autopsy not being obtained.

The skin over most of the areas examined appears normal. The scales are numerous and loose. In a few small areas there is excessive keratosis involving much of the Malpighian layer and here many cells show the peculiar changes described in Case 1. In many hair follicles and in all the sweat glands these peculiar changes were very marked.

**Case 7.**—(501.) The material from this case, furnished by Dr. Williams, consisted of several pieces of skin snipped off under cocaine from a child of three years, on the second day of a well-marked measles eruption of maculo-papular type. Fixation, Zenker's fluid. Stains by eosin and hematoxylin, methylene blue, gentian violet, and Gram's method.

Microscopical examination: There is general edema of the Malpighian layer and of the subepithelial connective tissue. There are many isolated necrosing homogenous epithelial cells and a few typical focal necroses, some of which are connected with subepithelial foci of round cells or altered sebaceous hair glands. Perinuclear vacuoles are prominent and there are many mitoses. A few flattened mononuclear leucocytes lie between the epithelia. The endothelium of the capillaries is swollen, proliferating, and many large round cells are packed in and about the capillaries. In many of the vacuoles of basal and other cells, in the lumina of capillaries, in the endothelium, in the large perivascular cells, and in the cells of the sweat glands, are basic-staining granules, rods, or rings similar to those described in Case 2. They are more prominent after methylene blue and still more so after gentian violet, and they are Gram-negative. Lesions in this case seem to be intermediate between those of Cases 2 and 3.

**Case 8.**—(499.) Material supplied by Dr. Williams, from a patient five years old, on the second day of eruption, from the skin of thigh.

The description of this case is very similar to that of the preceding one, but definite focal necroses were not found, rather numerous polynuclear leucocytes were present in the capillaries, and the peculiar granules and rings in vacuoles and cell bodies were much less numerous.

**Case 9.**—(502.) Material supplied by Dr. Williams. Child of eight months, third day of eruption, skin of chest.

Description similar in all respects to the one preceding, except that a very few early foci of necrosis were observed.

## EPICRITICAL.

The findings in the preceding cases indicate that the usual cutaneous lesions of measles are those enumerated under Case 3, appearing also in Cases 4 and 7, and consisting in: (1) focal necroses with the formation of small vesicles; (2) isolated necrotic epithelia; (3) diffuse perinuclear vacuolation of cells of epidermis and of dermal glandular structures; and (4) congestion, edema, swelling, and proliferation of endothelial cells, and moderate increase of large round cells (see Fig. 3).

In a case of hemorrhagic measles (Case 2) the focal necroses were wanting but all the other lesions mentioned above were present, and, in addition, in the vacuoles of the epithelium in all situations, and in and about the capillaries and lymph spaces were very large numbers of peculiar granules or ring-shaped structures. The nature of these bodies is left undetermined but the most probable hypothesis is that they represent a coagulated albuminous material derived from the blood and from degenerating epithelium. Apparently similar bodies in smaller numbers were noted in other cases (Cases 7 and 8).

In a case of nearly confluent measles eruption focal necrosis and perinuclear vacuolation were absent, and instead one finds hyperkeratosis and a peculiar form of degeneration of the Malpighian cells marked chiefly by the homogenization and fragmentation of cell bodies and nuclei with the appearance of very many peculiar geometrical and vacuolated structures. Such changes not having been found in other diseases, they may for the present be regarded as specific for certain cases of measles. Similar changes of less general distribution were found in a second case. Therefore at least three rather distinct series of histological lesions may be regarded as belonging to the eruption of measles. The commonest lesion encountered in the present study, focal necroses with formation of vesicles, appears to be essentially the same as those described by Catrin but very imperfectly recognized by previous writers. The deep "phlyctenes" of Catrin did not appear in the present series of cases. The exudation and infiltration in and about the hair follicles and sebaceous and sweat glands described by the older writers were present in some cases but absent in others, so that these changes can probably not retain the specific importance in the measles process which has been formerly attributed to them.

The perinuclear "boules colloides" of Catrin seem to be identical with the faintly staining homogeneous material in the perinuclear vacuoles of the present descriptions, but the former stained intensely with eosin, while in the material of the present study it proved faintly basophile. The larger conglomerate masses of colloid material described by Catrin seem to be referable to groups of necrotic epithelium, or else they were not encountered in my cases.

Since no single type of cellular changes is invariable in measles and since the lesions observed vary so widely, the question may arise whether the clinical diagnosis of measles as at present applied may not really cover more than one infection. This question seemed unavoidable when the peculiar changes observed in a case of hemorrhagic measles (Case 2) were found nearly duplicated in a case of *pityriasis rosea*. However, the clinical features of measles are extremely characteristic, and in view of this fact and of our ignorance of the etiological agent, it would seem that the occurrence of quite different epithelial changes would not warrant one in seriously urging that several infections are now passing under the term of "measles." In variola, primary hemorrhagic, diffuse or confluent, and discrete pustular forms, the minute changes in the epithelial cells are quite different, but the disease itself is almost certainly a single infection.

As with the other exanthems, measles is characterized by a severe inflammation of the pharynx and respiratory tract. Except for its very frequent complication with broncho-pneumonia, it does not appear to be as severe as that of scarlatina, or nearly as serious as that of variola, but, as with both of these maladies, it antedates the exanthem. In the present cases it consisted of an intense catarrhal inflammation with marked desquamation of cells, superficial erosions, minute focal ulcers, and extensive subepithelial infiltration with round cells. As in smallpox and scarlet fever the peculiar epithelial changes and structures seen in the skin are largely or wholly missing in the mucous membranes. If there is anything specific in these lesions of the mucous membranes it is the extensive subepithelial infiltration with round cells, which often shows a focal distribution, and the focal necroses, and it has seemed to me that the occurrence of the former probably determines the latter lesion in skin, pharynx, and respiratory tract. Koplik's spots seem to be one expression of this focal character of the process.

The lymphocytosis of measles is fully explained anatomically by the intense congestion and hyperplasia of the lymphoid tissues. The frequency of tuberculous sequelae in measles may perhaps be referred to the unearthing of buried tubercle bacilli from these lymph nodes. The internal organs in measles seem to exhibit little that is specific of the disease. In the livers examined there was considerable granular and fatty degeneration, and these changes were more intense in certain foci reaching at times the condition of the focal necroses described by Freeman.<sup>1</sup>

From the study of the present cases one may perhaps be warranted in theorizing briefly concerning the general nature of the virus of measles. In the writer's opinion all the indications drawn from these cases point to the existence in measles of an infection by an actively multiplying micro-organism of the class of bacteria. Although one finds in the epithelial cells many structures which bear some resemblance to protozoa and the origin of one group of these structures could not be satisfactorily determined, yet the general characters of the disease, and especially the widespread occurrence of very acute degeneration and necrosis of epithelial cells, all suggest that measles is referable to infection by a bacterium which produces an active toxin having special affinity for superficial epithelial cells.

#### DESCRIPTION OF PLATES 1 AND 2.

##### PLATE 1.

FIG. 1.—Confluent measles (Case 1). Fixation: Bichloride. Stain: Borrel's iodin green and fuchsin. Specimen shows excessive zone of keratosis, isolated necrotic cells, and a variety of curious bodies resulting from degeneration, vacuolation, or fragmentation of nuclei and cell bodies.

FIG. 2.—Hemorrhagic measles (Case 2). Fixation: Alcohol 50 per cent. Stain: Eosin and methylene blue. Specimen shows perinuclear vacuoles containing basophile granules, globules, rings, and elongated rods. Similar structures are seen in the cytoplasm, between the cells, and within the subepithelial vessels.

##### PLATE 2.

Common vesico-papule of measles (Case 3). Fixation: Zenker's fluid. Stain: Eosin and methylene blue. Specimen shows a small central area containing loose necrotic epithelia and serous exudate, surrounded by coherent necrotic cells. Beyond are isolated necrotic cells, perinuclear vacuoles, and peculiar perinuclear and cytoplasmic structures.

<sup>1</sup> *N. Y. Med. Jour.*, 1898, 54, p. 136; also *Studies from Dep't of Path., Coll. Phys. and Surg., N. Y.*, 1899, 7.

PLATE I

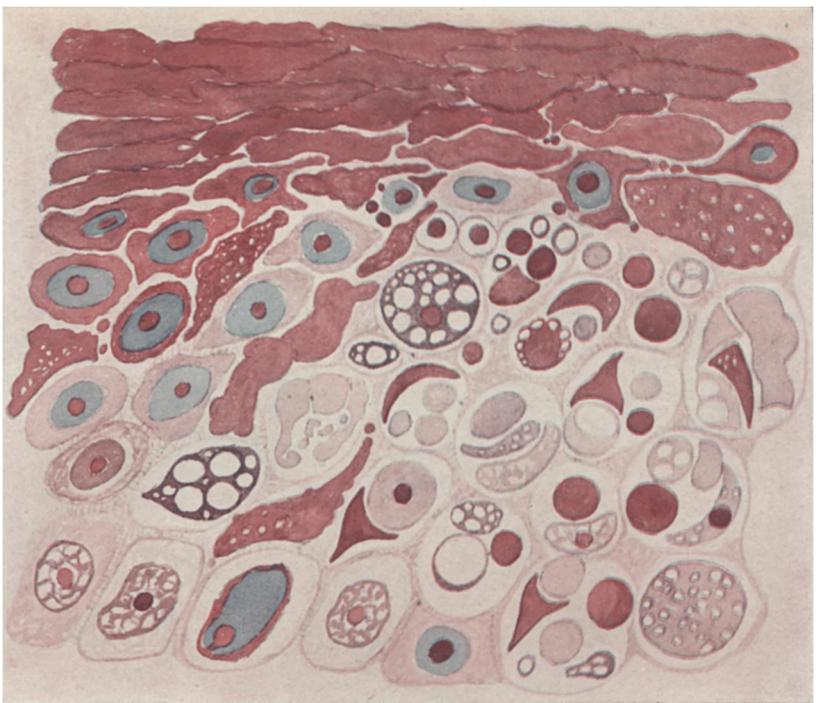


FIG. 1



FIG. 2

PLATE 2

